REMARKS

Claims 1-50 were previously pending in this Application. The Examiner has withdrawn claims 4-7, 15, 17, and 25-50 from consideration at this time. Applicant cancels herewith claims 28-38, 40, and 47-49. Applicant amends herewith claims 1-3, 12-14, and 21, and adds new claims 51-53 readable on the elected invention. Applicant also amends herewith withdrawn claims 4, 15, 39, 41-46, and 50. Thus, claims 1-27, 39, 41-46, and 50-53 are pending, and of these, claims 1-3, 8-14, 16, 18-24, and 51-53 are under examination at this time.

1. Summary of Claim Amendments

Applicant cancels herewith claims 28-38, and 40, directed to a pharmaceutical composition, and amends claims 39 and 41-46 to depend on elected claims. Applicant also cancels herewith claims 47-49, directed to a kit. Applicant reserves the right to pursue canceled subject matter in a continuation or divisional application claiming priority to the present Application.

Applicant amends claims 1, 2, 3, and 4 to recite "an effective amount of hyaluronidase and collagenase." Support for this amendment is provided in original claim 13, and on page 9, lines 4-15, of the Application as originally filed.

Applicant amends claims 12, 41-42, and 46 to recite an additional agent (*e.g.*, at least one, two, three or four agents) selected from other enzymes, anesthetics, vitamins, zinc, antibiotics, anti-allergic agents, carbamide, cytokinases, vasoconstrictors, anticlerical agents, anti-viral agents, anti-fungal agents, anti-inflammatory agents, and lubricants. Support for each of these additional agents is provided in the original claims and/or in the Application as originally filed; *e.g.*, "enzymes," "anesthetics," "vitamins," "antibiotics," and "anti-inflammatory agents" are recited in original claim 12; "anti-allergic agents," "carbamide," and "vasoconstrictors" are recited in original claim 39; "anticlerical agents" and "cytokinases" are recited in original claim 42; "lubricants" is recited in original claim 28; "anti-viral agents" and "anti-fungal agents" are provided on page 26, lines 19-20, of the Application as originally filed; and "zinc" is provided on page 27, line 2, of the Application as originally filed.

Applicant amends claim 13 to further comprise a polymer in the pharmaceutical composition of claims 1, 2, 3, and 4.

Applicant amends claim 14, dependent on claim 13, to define the polymer as methylcellulose, cellulose, polyvinylalcohol, or polyethylene glycol. Applicant similarly amends claim 43. Support for "cellulose" in amended claim 43 is provided in original claim 14. Support for "polyethylene glycol" in amended claims 14 and 43 is provided on page 27, line 14, of the Application as originally filed.

Applicant amends claim 15 to specify that the composition is a "liquid" rather than "in the form of eye drops." Support for a "liquid" pharmaceutical form is provided in original claim 32. Applicant also amends original claim 50 to depend from original claim 15, and defines the liquid composition recited therein as being in the form of a spray or eye drops.

Applicant adds new claim 51, dependent on claim 16, to further define the gel as a "semi-solid gel." Support for the term "semi-solid gel" is provided in original claim 33.

Applicant adds new claim 52, dependent on claims 1, 2, 3 or 4, to further define the contact lens as a "gas permeable" contact lens. Support for "gas permeable" is provided on page 23, lines 1-2, of the Application as originally filed.

Applicant adds new independent claim 53, directed to a method of treating presbyopia. Support for this new claim is provided in original claims 1, 13, and 24.

Applicant has also amended various claims to correct typographical errors, for example, "years" in claim 21 to "year", and "hypotonic" in claim 45 to "hypertonic". Other amendments to the claims are merely clerical in nature.

No new matter has been added to the Application by the present Amendment.

2. Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 1-3, 8, 9, 11-13, 18, 22, and 23 under 35 U.S.C. § 102(b) as being anticipated by European Patent Publication No. 0608341 (hereafter "Harris").

The Examiner points to page 2, lines 3-5, of Harris as teaching a method for accelerated corneal reshaping involving the use of an enzyme or other agent, such as hyaluronidase, to facilitate reshaping of the cornea to reduce or eliminate refractive errors of the eye. The Examiner points to page 3, line 39, to page 4, line 5, of Harris as teaching use of a contact lens in combination with a medicament, wherein the medicament permits reshaping of the cornea from a first configuration to a

second configuration in order to correct refractive errors in the eye. The Examiner points to page 5, lines 8-9, of Harris as teaching that when the lens is removed, the cornea is capable of maintaining the desired second configuration without the support of the lens. In particular, the Examiner finds that Harris teaches use of a medicament containing hyaluronidase to soften the cornea (page 6, line 32), and that the medicament may further comprise other agents such as anesthetics (page 3, lines 13-38), enzymes and enzyme activators (page 4, lines 6-21), and enzyme inhibitors (*e.g.*, cysteine and EDTA). The Examiner acknowledges that Harris does not teach the use of a polymer in the formulation. The Examiner further acknowledges that Harris does not teach a medicament useful in the treatment of presbyopia.

The Examiner points to page 4, lines 34-42, as specifically teaching use of collagenase, but nowhere in that section is collagenase mentioned. Harris, in fact, refers to collagenase only once, and only in the context of specifically dissuading one from using that enzyme (paragraph [0087] of Harris). Harris points only to matrix metalloproteinase-1 and matrix metalloproteinase-2 as corneal softening agents useful in breaking down collagen in the cornea (paragraph [0022] and page 7, Table II, of Harris). It is clear from the Applicant's specification that the term "collagenase" as claimed does not encompass these two enzymes (page 24, lines 24-31 to page 25, lines 1-2, of the Application as originally filed).

To anticipate a claim, the reference must teach each and every element of the claim (MPEP 2131). Applicant amends the pharmaceutical composition recited in claims 1 to 3 to comprise an effective amount of hyaluronidase and collagenase. Since Harris does not teach the combination of hyaluronidase and collagenase, Harris does not anticipate amended claims 1-3, 8, 9, 11-13, 18, 22, and 23. Applicant respectfully requests that this rejection under § 102 be withdrawn.

3. Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 10, 14, 16, 19-21 and 24 under 35 U.S.C. § 103(a) as being obvious over Harris in view of U.S. Patent Appl. Publication No. 2005/0080484 (hereafter "Marmo"). As discussed above, Harris does not teach the use of a polymer in the formulation or the treatment of presbyopia. The Examiner cites Marmo to remedy this deficiency in Harris.

The Examiner points to the Abstract and paragraphs [0003] and [0009] of Marmo as teaching methods and devices for improving vision comprising a corrective ocular device, such as a corneal appliance that is placed over an eye and has a lens body. The Examiner points to paragraph [0065] of Marmo as teaching that the lens may be structured to correct visual deficiencies such as presbyopia. The Examiner points to paragraphs [0108] and [0109] of Marmo as teaching use of a gel having at least one water soluble or water swellable polymeric material, such as hydroxymethylcellulose. The Examiner concludes one skilled in the art acquainted with Harris and the above teachings of Marmo would be led with a reasonable expectation of success to the claimed invention. Applicant respectfully disagrees and submits that the claims are non-obvious over Harris alone or in combination with Marmo for the following reasons.

Applicant submits that one skilled in the art, seeking to improve upon the teachings of Harris, would not look to Marmo for guidance. Harris is directed to the field of enzyme orthokeratology, *i.e.*, a non-surgical technique using a combination of contact lenses and enzymes for corneal reshaping to reduce or eliminate refractive errors of the eye. Marmo has nothing to do with enzyme orthokeratology and, in fact, does not teach the use of enzymes for correcting refractive errors of the eye. Marmo merely teaches a surgical technique involving cutting a "flap" or "pocket" beneath the epithelium of the cornea wherein a lens is inserted. The "gel" and "water soluble or water swellable polymeric material" of Marmo described in paragraphs [0108] and [0109] is used to more effectively separate the epithelium of the cornea from Bowman's membrane prior to placement of the lens. The surgically implanted lens of Marmo may be a "vision correcting lens" to treat visual deficiencies.

Thus, Applicant submits that claims 10, 14, 16, 19-21, and 24 are not obvious over Harris in combination with Marmo because there is simply no motivation to combine the two references. One skilled in the art, seeking to improve on the non-surgical method of Harris, would certainly not be led to a reference which describes surgical methods, let alone motivated to combine the two to arrive at the presently claimed invention. The fact that Marmo teaches use of a polymer and treatment of presbyopia is irrelevant considering both of these features are involved in the placement of or use of a surgically implanted lens.

Should the Examiner be minded to further reject claims 1-3, 8, 9, 11-13, 18, 22, and 23 for obviousness, Applicant submits that neither Harris nor Marmo teach, suggest, or provide any motivation to use a combination of hyaluronidase and collagenase. As discussed above, the medicament described by Harris requires hyaluronidase and optionally a number of other corneal softening agents, such as matrix metalloproteinase-1 and matrix metalloproteinase-2 (paragraph [0022] and page 7, Table II, of Harris), and the only reference to collagenase in Harris specifically teaches away from use of that enzyme (paragraph [0087] of Harris). Furthermore, all of the "working" formulations taught in Harris only include hyaluronidase as the singular enzyme in the formulation, see, *e.g.*, the hyaluronidase formulations described in paragraphs [0036], [0037], and [0039] of Harris. Thus, Applicant submits that one skilled in the art, seeking to improve on Harris, might be led to combine hyaluronidase with matrix metalloproteinase-1 or matrix metalloproteinase-2, but would not be led to combine hyaluronidase and collagenase, as presently claimed.

Researchers have worked for many years to develop orthokeratology for long term correction of refractive error. Applicant has found that a combination of contact lenses and an enzymatic formulation comprising hyaluronidase and collagenase is effective in treating low to moderate vision problems such as presbyopia, myopia, hyperopia, and astigmastism. In contrast to Harris, which teaches actually injecting the hyaluronidase formulation into the cornea, the present invention teaches a completely non-invasive therapy wherein the enzymatic formulation is administered topically to the eye as a gel or liquid.

Applicant submits that the claims are not obvious in view of Harris alone or in combination with Marmo. Applicant respectfully requests this rejection under § 103 be withdrawn.

In view of the above Amendment and Remarks, Applicant believes the pending Application is in condition for allowance.

If additional fees are due, please charge our Deposit Account No. 23/2825, under Docket No. O0327.70000US00, from which the undersigned is authorized to draw.

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Respectfully submitted,

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